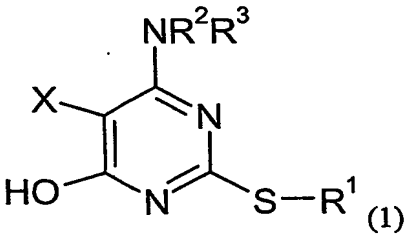
CLAIMS

1. A compound of formula (1), a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:



(1)

wherein R^1 is a group selected from C_{3-7}carbocyclyl, C_{1-8}alkyl, C_{2-6}alkenyl and C_{2-6}alkynyl; wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from fluoro, nitrile, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, phenyl or heteroaryl; wherein phenyl and heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, C_{1-6}alkyl and trifluoromethyl;

wherein R^2 is C_{3-7}carbocyclyl, optionally substituted by 1, 2 or 3 substituents independently selected from:

(a) fluoro, $-OR^4$, $-NR^5R^6$ $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$;

(b) a 3-8 membered ring optionally containing 1, 2 or 3 atoms selected from O, S, $-NR^8$ and whereby the ring is optionally substituted by C_{1-3}alkyl or fluoro; or

(c) phenyl or heteroaryl, each of which is optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-NR^8COR^9$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, C_{1-6}alkyl and trifluoromethyl;

or R^2 is a group selected from C_{1-8}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl wherein the group is substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, *N*-(C_{1-6}alkyl)-*N*–(phenyl)amino, *N*-C_{1-6}alkylcarbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, *N*-(C_{1-6}alkyl)-*N*–(phenyl)carbamoyl, carboxy, phenoxycarbonyl, $-NR^8COR^9$, $-SO_2R^{10}$, $-SO_2NR^5R^6$ and $-NR^8SO_2R^9$;

wherein R^3 is hydrogen or R^2;

R^4 is hydrogen or a group selected from C_{1-6}alkyl and phenyl, wherein the group is optionally substituted by 1 or 2 substituents independently selected from halo, phenyl, $-OR^{11}$ and $-NR^{12}R^{13}$;

R^5 and R^6 are independently hydrogen or a group selected from C_{1-6}alkyl and phenyl wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, $-OR^{14}$,$-NR^{15}R^{16}$, $-CONR^{15}R^{16}$, $-NR^{15}COR^{16}$, $-SONR^{15}R^{16}$ and $NR^{15}SO_2R^{16}$

or

R^5 and R^6 together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by 1, 2 or 3 substituents independently selected from phenyl, $-OR^{14}$, $-COOR^{14}$, $-NR^{15}R^{16}$, $-CONR^{15}R^{16}$, $-NR^{15}COR^{16}$, $-SONR^{15}R^{16}$, $NR^{15}SO_2R^{16}$ or C_{1-6}alkyl (optionally substituted by 1 or 2 substituents independently selected from halo, $-NR^{15}R^{16}$ and $-OR^{17}$ groups);

R^{10} is hydrogen or a group selected from C_{1-6}alkyl or phenyl, wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, $-OR^{17}$ and $-NR^{15}R^{16}$; and

each of R^7, R^8, R^9, R^{11}, R^{12}, R^{13}, R^{14} R^{15}, R^{16}, R^{17} is independently hydrogen, C_{1-6}alkyl or phenyl;

X is hydrogen, halo, cyano, nitro, hydroxy, C_{1-6}alkoxy (optionally substituted by 1 or 2 substituents selected from halo, $-OR^{11}$ and $-NR^{12}R^{13}$), $-NR^5R^6$, $-COOR^7$, $-CONR^5R^6$, $-NR^8COR^9$, thio, thiocyano, thioC_{1-6}alkyl (optionally substituted by 1 or 2 substituents selected from halo, $-OR^{17}$, $-COOR^7$,$-NR^{15}R^{16}$, $-CONR^5R^6$), $-SO_2R^{10}$, $-SO_2NR^5R^6$ $-NR^8SO_2R^{10}$or a group selected from C_{3-7}carbocyclyl, C_{1-8}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl, wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$ and $-NR^8SO_2R^9$; or a –phenyl, -heteroaryl, -thiophenyl, -thioheteroaryl, aminoheteroaryl, and thioC_{1-6}alkylheteroaryl group, all of which may be optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, $-OR^4$, $-NR^5R^6$, $-CONR^5R^6$, $-COOR^7$, $-NR^8COR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-SO_2NR^5R^6$, $-NR^8SO_2R^9$, C_1-C_6alkyl, phenyl, heteroaryl or trifluoromethyl groups;

2. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein R^1 is C_{1-8}alkyl optionally substituted by 1, 2 or 3 substituents independently selected from phenyl or heteroaryl, wherein phenyl and heteroaryl

are optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, -OR^4, -SR^{10}, C_{1-6}alkyl and trifluoromethyl.

3. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein R^2 is C_{1-8}alkyl substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, *N*-(C_{1-6}alkyl)-*N*–(phenyl)amino, *N*-C_{1-6}alkylcarbamoyl, *N,N*-di(C_{1-6}alkyl)carbamoyl, *N*-(C_{1-6}alkyl)-*N*–(phenyl)carbamoyl, carboxy, phenoxycarbonyl, –NR^8COR^9, –SO_2R^{10}, –$SO_2NR^5R^6$ and –$NR^8SO_2R^9$; andwherein R^3 is hydrogen;

4. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein R^4, R^5, R^6, R^8, R^9 and R^{10} are independently hydrogen, C_{1-4}alkyl or phenyl.

5. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:,wherein X is hydrogen, halo, cyano, nitro, hydroxy, thio, thiocyano, -$CONR^5R^6$, thioC_{1-6}alkyl (optionally substituted by 1 or 2 substituents selected from halo, -OR^{17}, -$NR^{15}R^{16}$, -$CONR^5R^6$), -$NR^8SO_2R^{10}$, C_{1-8}alkyl (optionally substituted by 1, 2 or 3 substituents independently selected from halo, -OR^4, -NR^5R^6, -$CONR^5R^6$, -$COOR^7$, -NR^8COR^9, -SR^{10}, -SO_2R^{10}, -$SO_2NR^5R^6$ and -$NR^8SO_2R^9$), heteroaryl, thioheteroaryl or thioC_{1-6}alkylheteroaryl all of which may be optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR^4, -NR^5R^6, -$CONR^5R^6$, -$COOR^7$, -NR^8COR^9, -SR^{10}, -SO_2R^{10}, -$SO_2NR^5R^6$, -$NR^8SO_2R^9$, C_{1-6}alkyl or trifluoromethyl.

6. A compound according to claim 2 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein R^1 is benzyl optionally substituted by 1 or 2 substituents independently selected from fluoro, chloro, bromo, methoxy, methyl and trifluoromethyl

7. A compound according to claim 3 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein R^2 is C_{1-4}alkyl, substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C_{1-6}alkoxy, C_{1-6}alkylamino, and di(C_{1-6}alkyl)amino; andR^3 is hydrogen;

8. A compound according to claim 4 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:, wherein X is hydrogen, fluoro, chloro, bromo, thiocyano, -$NR^8SO_2R^9$ (where R^8 is hydrogen and R^9 is methyl) –thioimidazolyl, -thiotriazolyl, -$CONH_2$, -$CONMe_2$ or cyano.

9. A compound selected from the group consisting of:
2-(Benzylthio)-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
2-(Benzylthio)-5-chloro-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
2-[(3-Chlorobenzyl)thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
5-Chloro-2-[(3-chlorobenzyl)thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
2-[(3-Chlorobenzyl)thio]-4-hydroxy-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-pyrimidinyl thiocyanate,
N-(2-[(3-Chlorobenzyl)thio]-4-hydroxy-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-pyrimidinyl)methanesulfonamide,
2-[(3-Chlorobenzyl)thio]-5-fluoro-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
2-[(2,3-difluorobenzyl)thio]-4-hydroxy-6{[(1S)-2-hdroxy-1-methylethyl]amino}pyrimidine-5-carbonitrile,
5-Chloro-2-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-4-pyrimidinol,
2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-iodo-4-pyrimidinol,
2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-nitro-4-pyrimidinol,
2-[[(3-Chlorophenyl)methyl]thio]-6-[[(1R)2-hydroxy-1-methylethyl]amino]-5-(1,3,4-thiadiazol-2-ylthio)-4-pyrimidinol,
2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1R)-2-hydroxy-1-methylethyl]amino]-5-(1*H*-imidazol-2-ylthio)-4-pyrmidinol,
2-[[(2,3-Difluorophenyl)methyl]thio]-5-[[2-(dimethylamino)ethyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-4-pyrimidinol,
1-[2-[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]- 4(1*H*)-pyridinethione,
2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-(4-pyridinylthio)- 4-pyrimidinol,

2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-(1*H*-1,2,4-triazol-3-ylthio)- 4-pyrimidinol,

2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(4-methyl-4*H*-1,2,4-triazol-3-yl)thio]- 4-pyrimidinol,

5-[(5-Amino-4*H*-1,2,4-triazol-3-yl)thio]-2-[[(2,3-difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]- 4-pyrimidinol,

2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[[5-(4-pyridinyl)-1,3,4-oxadiazol-2-yl]thio]- 4-pyrimidinol,

Ethyl[[2-[[(2,3-difluorophenyl)methyl]thio]-4-hydroxy-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]- AcOH,

2-[[2-[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]-*N*-methyl- acetamide,

2-[[2-[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]-*N*-[2-(dimethylamino)ethyl]- acetamide,

1-[[[2-[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]acetyl]-piperazine,

2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(4-methyl-2-oxazolyl)thio]- 4-pyrimidinol,

2-[[(2,3-Difluorophenyl)methyl]thio]-6-[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(1,2,4-oxadiazol-3-ylmethyl)thio]- 4-pyrimidinol,

2-[(2,3-difluorobenzyl)thio]-4-{[(1*R*)-1,2-dihydroxyethyl]amino}-6-hydroxypyrimidine-5-carboxamide,

2-[(2,3-difluorobenzyl)thio]-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}-5-(5-methyl-1,2,4-oxadiazol-3-yl)pyrimidin-4-ol,

2-[(2,3-difluorobenzyl)thio]-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}-5-(1,3-oxazol-5-yl)pyrimidin-4-ol,

2-[(2,3-difluorobenzyl)thio]-4-{[(1*R*)-1,2-dihydroxyethyl]amino}-6-hydroxy-*N*,*N*-dimethylpyrimidine-5-carboxamide,

2-[(2,3-difluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}-pyrimidin-4-ol,

2-[(3,4-difluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}-pyrimidin-4-ol,

2-[(3-fluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}pyrimidin-4-ol, or

2-[(4-fluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}pyrimidin-4-ol and a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof.

10. A compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament.

11. A compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

12. A compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of cancer.

13. A compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of COPD.

14. The use of a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of human diseases or conditions in which modulation of chemokine receptor activity is beneficial.

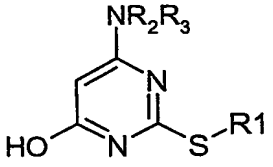
15. The use of a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

16. The use of a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of cancer

17. A pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9; and a pharmaceutically-acceptable diluent or carrier.

18. A process for the preparation of a compound of formula (1) as defined above which comprises

(a) treating a compound of formula (2):



(2)

wherein R^1, R^2 and R^3 are as defined in formula (1), with suitable electrophiles.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups;

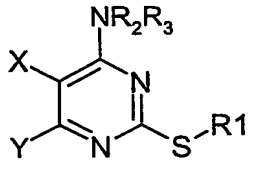
ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

(iv) forming a prodrug

(v) forming an in vivo hydrolysable ester; or

(b) , where X is 1,3-oxazol-5-yl by treating a compound of formula (4):



(4)

wherein R^1, R^2 and R^3 are as defined in formula (1), X is –CHO and Y is protected hydroxy by treatment with *p*-toluenesulfonylmethyl isocyanide and potassium hydroxide in refluxing methanol.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups;

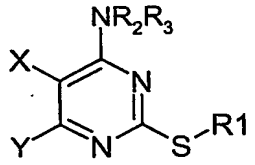
ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

(iv) forming a prodrug,

v) forming an *in vivo* hydrolysable ester; or

(c) where X is CN by treating a compound of formula (4):



(4)

wherein R^1, R^2 and R^3 are as defined in formula (1), X is CN and Y is halogen by treatment with potassium *tert*-butoxide in refluxing aqueous toluene.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups,

ii) converting the compound of formula (1) into a further compound of formula (1),

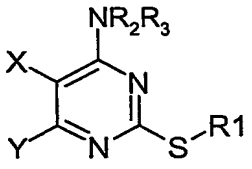
iii) forming a salt;

(iv) forming a prodrug,

v) forming an *in vivo* hydrolysable ester; or

(d) where X is $-CONR^5R^6$ by;

c) treating a compound of formula (4):



(4)

wherein R^1, R^2 and R^3 are as defined in formula (1), X is $-CONR^5R^6$ and Y is halogen with a suitable base.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups;

ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

(iv) forming a prodrug,

v) forming an *in vivo* hydrolysable ester.

19. A combination therapy which comprises administering a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, or a pharmaceutical composition or formulation comprising a compound of formula (1), concurrently or sequentially with other therapy and/or another pharmaceutical agent.

20. A combination therapy as claimed in claim 19 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

21. A combination therapy as claimed in claim 19 for the treatment of cancer.

22. A pharmaceutical composition which comprises a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, in conjunction with another pharmaceutical agent.

23. A pharmaceutical compositon as claimed in claim 22 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

24. A pharmaceutical composition as claimed in claim 22 for the treatment of cancer.